In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 15-1146V
Filed: March 3, 2017

JESSICA REAPE,	*	
	*	Special Master Sanders
Petitioner,	*	
v.	*	Entitlement; Decision on the Record;
	*	Insufficient Proof of Causation;
SECRETARY OF HEALTH	*	Influenza ("Flu" or "Flumist") Vaccine;
AND HUMAN SERVICES,	*	Tourette's syndrome ("TS").
	*	
Respondent.	*	

Daniel J. Mannix, Muller, Mannix & Hobbs, PLLC, Glen Falls, NY, for Petitioner.
Christine M. Becer, United States Department of Justice, Washington, DC, for Respondent.

DECISION ON ENTITLEMENT[1]

On October 7, 2015, Jessica Reape ("Petitioner") filed a petition pursuant to the National Vaccine Injury Compensation Program.[2] Petitioner alleged that the administration of the Flumist ("Influenza" or "Flu") vaccine she received on September 25, 2012 caused her to develop Tourette's syndrome ("TS").

Based on the medical records and expert reports, the undersigned finds that Petitioner is not entitled to compensation under the Vaccine Act.

I. Procedural History

[1]This decision shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted decision. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] The Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-10 et seq. (hereinafter "Vaccine Act," "the Act," or "the Program"). Hereafter, individual section references will be to 42 U.S.C. § 300aa of the Act.

Petitioner filed eight exhibits with her petition on October 7, 2015. *See* Petitioner's Exhibits ("Pet'r's Exs.") 1-9, ECF No. 1. An exhibit comprised of Petitioner's expert's medical records was filed two days later. Pet'r's Ex. 6, ECF No. 7. The case was initially assigned to Special Master Hamilton-Fieldman. Notice of Assignment, ECF No. 4. From November 9-12, 2015, six additional exhibits consisting of medical records were filed, followed by a statement of completion on November 17, 2015. Pet'r's Exs. 10-15; Statement of Completion, ECF No. 19.

Respondent filed a Rule 4(c) Report on January 6, 2016, in which he recommended against compensating Petitioner for the allegedly vaccine caused injury. *See* Respondent's Report ("Resp't's Report"), ECF No. 21. Respondent averred that Petitioner had failed to identify a medical theory that connects the Flumist vaccine to TS. *Id.* at 7. Furthermore, Respondent noted that when Petitioner presented to her primary physician, Petitioner was referred to a movement disorder specialist, who "diagnosed [P]etitioner with a conversion disorder,[3] unrelated to vaccination." *Id.*

A Rule 5 status conference was held on January 28, 2016. *See* Unnumbered Minute Entry (January 28, 2016). Petitioner's counsel indicated that Petitioner was still experiencing symptoms, although they had lessened. *See* Scheduling Order, filed January 29, 2016. Petitioner filed an expert report and medical literature shortly before the status conference, therefore Respondent was unable to discuss these filings. Pet'r's Expert Report, filed January 28, 2016. Respondent wanted to review Petitioner's expert report and requested time to file a responsive expert report. Scheduling Order, ECF No. 22. In the scheduling order following the status conference, Special Master Hamilton-Fieldman set deadlines for Respondent's responsive expert report and Petitioner's responsive supplemental expert report. *Id.*

Respondent filed his expert report, as well as supportive medical literature, on April 1, 2016. Resp't's Exs. A (expert report), B (medical literature). Petitioner's deadline to file a responsive supplemental expert report was on May 6, 2016. After Petitioner missed this deadline, Chambers contacted Petitioner twice to inquire about the expert report. *See* Unnumbered Docket Entries Noting Informal Communication (May 10, 2016 and May 12, 2016).

On May 13, 2016, Petitioner filed a status report notifying the Court that she did not intend to file a responsive supplemental expert report, and that she wished to move for a ruling on the record. Pet'r's Status Report, ECF No. 25. Petitioner requested that the Court "set a schedule for the motion that would allow for the filing of [her] moving papers in early to mid-July, 2016." *Id.* After considering Petitioner's request, Special Master Hamilton-Fieldman ordered Petitioner to move for a ruling on the record by July 8, 2016. Scheduling Order, filed May 13, 2016. Special Master Hamilton-Fieldman also set deadlines for Respondent's response to the motion and Petitioner's reply to the response. *Id.*

[3] Conversion disorder is a mental disorder characterized by symptoms, including loss or alteration of voluntary motor or sensory functioning suggesting physical illness, such as seizures, having no demonstrable physiological basis. DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 549 (32nd ed. 2012) [hereinafter DORLAND'S].

Petitioner filed a Motion for Decision on the Record ("Motion") on July 8, 2016. Pet'r's Motion for Decision on the Record, ECF No. 28. In the Motion, Petitioner referenced filed medical records and expert report supporting Petitioner's alleged TS. *Id.* Three days later, Petitioner filed a PubMed abstract and an excerpt from an article as attachments to her Motion. *See* ECF No. 29, filed July 11, 2016.

On August 10, 2016, Respondent filed a response arguing that Petitioner failed to satisfy her burden under the *Althen* prongs. Resp't's Response to Motion ("Response"), ECF No. 31. First, Respondent avers that Petitioner's theory of vaccine causation is not supported by reliable scientific evidence. Second, Respondent argues that because Petitioner "cannot demonstrate that the Flumist vaccine can cause TS, it logically follows that she has not established a logical sequence of events in her case." *Id.* Third, Respondent argues that Petitioner has not offered any evidence to establish that seventeen days "is a medically appropriate time-period" for TS onset. *Id.* at 6. Additionally, Respondent states that Petitioner did not show that the "Flumist vaccine was a "but for" cause and a substantial factor in bringing about her alleged injury." *Id.* at 6. Lastly, because Petitioner did not meet "her statutory burden of establishing a prima facie case for entitlement, the burden never shift[ed] to Respondent to prove an alternative cause." *Id.* at 6. Thereafter, Petitioner did not file a reply.

On January 11, 2017, the case was reassigned to the undersigned. *See* Notice of Reassignment, ECF No. 33. On February 21, 2017, the undersigned ordered Petitioner to file an affidavit stating that she is aware "(1) Petitioner filed a Motion for a Decision on the Record; (2) a Decision on the Record is based solely on the documents filed for the record; (3) Dr. Trifiletti did not write a supplemental expert report in response to Dr. Gilbert's expert report; and (4) the undersigned will issue a Decision on the Record accordingly." *See* Order, ECF No. 36. Petitioner did not file the affidavit. Petitioner's counsel did, however, file an affidavit representing that he had informed his client of the aforementioned facts. Pet'r's Ex. 16. This matter is now ripe for a decision on entitlement.

II. Summary of the Relevant Evidence

a. Medical Records

Petitioner received the Flumist vaccine on September 25, 2012, as a condition of her employment as a nurse case manager. *See* Pet'r's Ex. 11 at 7; Pet'r's Ex. 2. She was thirty years old at the time of vaccination, and her past medical history is significant for depression and anxiety. Pet'r's Ex. 3 at 2.

Petitioner avers that approximately 17 days later, on October 12, 2012, she "suddenly developed uncontrollable muscle movements in her limbs and head." Pet. at 1. Petitioner also avers that these "symptoms progressed in intensity and frequency" for three days, and that she experienced uncontrollable "shaking of the head from side to side . . . uncontrollable knee jerks, and mild vocal tics." *Id.* at 1-2. On October 15, 2012, Petitioner presented to primary care physician, Dr. Karen Williams. Pet'r's Ex. 3 at 2. Petitioner complained of "electrical like pulses through her body" and stated she could not make the movements stop. *Id.* Petitioner

reported that "2 years ago her sister started with the same symptoms" and then was recently diagnosed with probable MS. *Id.* She also reported that her mother has a seizure disorder. *Id.*

A complete review of systems was negative. *Id.* Dr. Williams noted that on exam, Petitioner was upset, tearful, and very emotional. *Id.* Dr. Williams also noted that Petitioner had repeated myoclonus[4] throughout the exam, with uncontrollable jerking and twitching. *Id.* at 3. Dr. Williams stated that when she left the exam room, Petitioner had no irregular movement, but started again as soon as Dr. Williams re-entered the room. *Id.* It is not clear from the medical records how Dr. Williams knew that Petitioner stopped moving after her exit. Dr. Williams commented in her report that Petitioner "is extremely anxious today and the more upset she gets, the worse the jerking movements are." *Id.* Dr. Williams also reported that when Petitioner left the exam room, she was able to walk to the restroom and the front desk without any jerking movements, but she did have one episode of her trunk jerking forward after she checked out. *Id.* Again, it is unclear from the medical records whether Dr. Williams or her staff observed this. Dr. Williams prescribed alprazolam to relax Petitioner's muscles and ease her anxiety. *Id.*

Later that same day, Petitioner's husband drove her to the emergency room at Upstate University Hospital, where she was admitted due to worsening symptoms. Pet. at 2. The review of systems was positive for "[j]erking and twitching movements getting worse and interfering with walking, talking." Pet'r's Ex. 4 at 7. During her physical exam, she displayed severe uncontrollable jerking and flailing movements. *Id.* at 8. Petitioner was also very anxious with pressured speech. *Id.* at 9. The ER physician noted that Petitioner was neurologically intact and able to ambulate. *Id.* at 8. Her labs were normal and a head CT was negative. *Id.* at 9. Petitioner was given an IV dose of valium which did suppress the movements, and she was admitted for neurological evaluation. *Id.* Dr. Izadyar, the evaluating neurologist, opined that Petitioner's movements were consistent with an adult-onset tic, as seen in TS. *Id.* at 71. He noted, however, that there were several atypical features, including Petitioner's late age of onset (TS usually happens in patients younger than 15 years of age) and a rapid progression of the tics. *Id.* As such, Dr. Izadyar concluded that the atypical features, along with a "lack of any systemic findings in the exam or screening labs, still leaves the diagnosis of somatoform disorders in the list of differential diagnosis." *Id.* He also noted that because Petitioner was a registered nurse, she was likely familiar with tics, TS, and PANDAS[5] before he discussed the diagnosis with her. *Id.* Dr. Izadyar noted that Petitioner referred to cases broadcasted in the media, where patients were initially diagnosed with conversion disorder, and later diagnosed with TS. *Id.*

[4] Myoclonus refers to shocklike contractions of a portion of a muscle, an entire muscle, or a group of muscles, restricted to one area of the body or appearing synchronously or asynchronously in several areas. DORLAND'S, at 1222.

[5] Pediatric autoimmune neuropsychiatric disorders associated with Group A Streptococci (PANDAS) is characterized by sudden and dramatic onset or exacerbation of obsessive-compulsive disorder (OCD) or tic symptoms, associated neurologic findings, and a recent streptococcal infection. NELSON TEXTBOOK OF PEDIATRICS 81 (19th ed. 2011).

Petitioner was discharged from the hospital on October 19, 2012. *Id.* at 32. Petitioner's brain MRI, neck CT, EEG, and rheumatological labs were normal. *Id.* at 32. Her primary discharge diagnosis was "[a]bnormal jerking and walking movements and vocal tics, potentially secondary to TS versus a psychogenic disorder." *Id.* Dr. Dragos Mihaila, a movement disorder specialist, saw Petitioner while she was hospitalized. It is unclear from the records precisely when he saw Petitioner during her hospital stay. It is also unclear whether Dr. Mihaila played a role in making the hospital's discharge diagnosis of "Tourette's versus psychogenic." *Id.* at 32-33. Petitioner was able to suppress involuntary movements when distracted or stimulated in another direction. *Id.* at 33. Biofeedback therapy was scheduled with a psychologist and she was instructed to return to Dr. Mihaila as an outpatient. *Id.* Petitioner was prescribed clonazepam[6] and zoloft.[7] *Id.* at 33.

After being released from the hospital without resolution of her symptoms, Petitioner "began to seek answers on her own." Pet. at 5. Petitioner's research led her to a conclusion that there were "similarit[ies] between [her] symptoms and Desiree Jennings[']s who was diagnosed with Dystonia Disorder after 10 days of the flu vaccine." Pet'r's Ex. 1 at 2. Petitioner's research also led her to Dr. Trifiletti, a pediatric neurologist specializing in the diagnosis and treatment of PANDAS. *Id.*; Pet'r's Ex. 6 at 10. It is unclear from the records when Petitioner saw Dr. Trifiletti. Petitioner did, however, fill out initial intake forms on November 5, 2012. *Id.* at 2-9. In 2012, on a date unspecified in the records, Dr. Trifiletti ordered twenty-one lab tests. Pet'r's Ex. 6 at 12.

On November 14, 2012, Petitioner had a follow-up visit with Dr. Mihaila. Pet'r's Ex. 5 at 2. Dr. Mihaila reported that Petitioner's clinical picture "resembled motor and vocal tics." *Id.* He also reported that an extensive work-up was done in the hospital to rule out an organic cause for tourettism. *Id.* Dr. Mihaila noted that the symptoms developed seventeen days after the flu vaccine. *Id.* It is unclear from the medical records whether this is an observation independently made by Dr. Mihaila or from what Petitioner told him. Since her hospital discharge, Petitioner continued to have vocalizations and abnormal movements of the head, face, arms, and legs. *Id.* She had one session with a psychotherapist for biofeedback, which she did not find useful. *Id.* The medical records are unclear as to when the psychotherapist appointment took place. Petitioner reported seeing Dr. Trifiletti, although it is not clear from the records when she saw him. *Id.* On exam, her movements appeared voluntary in nature and were suppressible briefly by her. *Id.* at 3. Since there had been no abnormalities on imaging and extensive laboratory work-up, the assessment was that she "most likely [had] a conversion disorder." *Id.*

On November 20, 2012, Dr. Trifiletti emailed Petitioner with the lab results. Pet'r's Ex. 7. Dr. Trifiletti indicated that most of the results were negative, but mycoplasma titers showed an elevated IgG and low IgM, Petitioner had positive Coxsackie titers, and elevated EBV capsid

[6] Clonazepam is used as an anticonvulsant in the treatment of Lennox-Gastaut syndrome and of atonic and myoclonic seizures, and as an antipanic agent in the treatment of panic disorders. DORLAND'S, at 373.

[7] Zoloft or sertraline hydrochloride is used for the treatment of major depressive disorder. PHYSICIAN'S DESK REFERENCE 2466-76 (66th ed. 2012).

IgG and EBV nuclear IgG. Pet'r's Ex. 7 at 2-5. Dr. Trifiletti advised Petitioner that he had a "reasonable suspicion that there was active or chronic mycoplasma and/or Coxsackie infection that was activated by the influenza vaccine." *Id.* at 3. Dr. Trifiletti recommended Biaxin and Valtrex as treatment, which Petitioner started. Four days later, she noticed a significant improvement. *Id.*; Pet'r's Ex. 9 at 2. By the eighth day of treatment, Petitioner averred she was free of Tourette symptoms. Pet'r's Ex. 9 at 2.

On December 7, 2012, Petitioner wrote an email to Dr. Trifiletti and reported that the previous night, she started having the "same symptoms as when this all started." *Id.* Petitioner wrote that she "did not stop moving" all night. *Id.* Petitioner included a timeline of her medications and indicated that she saw improvement when she was on an antiviral. *Id.* The record is silent as to whether Dr. Trifiletti responded to Petitioner's email. On March 7, 2013, Petitioner established primary care with Dr. Julie LaPointe. Pet'r's Ex. 12 at 24. Dr. LaPointe reported Dr. Trifiletti's findings from a genetic screening he ordered. Dr. Trifiletti found a mutation in the NLN gene, which he stated relates to Tourette's. *Id.* Dr. LaPointe noted that Petitioner had a "Tourette reaction to nasal flu spray." It is unclear whether Dr. LaPointe is relaying what Petitioner told Dr. LaPointe or vice versa. Dr. LaPointe also noted that Petitioner reported continued vocal tics and twitching at night, and when tired. *Id.* On August 22, 2013, Dr. LaPointe stated that Petitioner "[r]eports that she continues to have multiple [psychological] stressors." *Id.* at 18. On September 11, 2013, Dr. LaPointe logged a phone conversation with Petitioner's psychiatrist at Upstate Hospital, who diagnosed Petitioner as having conversion disorder. *Id.* at 17. It is not clear from the medical records the exact date Petitioner was diagnosed by this psychiatrist, but the psychiatrist states that "she has been unable to get in contact with [Petitioner]." *Id.* On April 23, 2015, Dr. LaPointe noted that Dr. Trifiletti diagnosed Petitioner with an inability to metabolize glutamate.[8] *Id.* at 4. Furthermore, Dr. Trifiletti instructed Petitioner to take dextromethorphan[9] as needed when exposed to monosodium glutamate (MSG). *Id.* Petitioner stated to Dr. LaPointe that after trying this, she "was very pleased with results to reverse the toxicity that she gets from MSG which presents as Tourette's." *Id.*

On July 23, 2013, Petitioner saw Dr. Mohiuddin at North Country Neurology for a second opinion. Pet'r's Ex. 14 at 3. Petitioner reported that sixteen days after a flu vaccination, she developed motor and phonetic tics. *Id.* at 3. Dr. Mohiuddin reviewed the extensive work-up at the hospital and Dr. Trifiletti's lab results, which found labs positive for persistent Coxsackie titers. *Id.* Dr. Trifiletti considered the Coxsackie titers to be rare in adults and a trigger of PANS.[10] Petitioner informed Dr. Mohiuddin that Dr. Trifiletti treated her with Biaxin and

[8] Glutamate is a salt, ester, or anionic form of glutamic acid; glutamate is the principal excitatory neurotransmitter in the central nervous system. DORLAND'S, at 790.

[9] Dextromethorphan is a nonopioid, synthetic derivative of morphine that acts on the cough center to suppress the cough reflex, used as an antitussive; administered orally. DORLAND'S, at 505.

[10] Pediatric acute-onset neuropsychiatric syndrome (PANS) is a condition similar to PANDAS with symptoms that include anxiety, movement abnormalities and sleep disturbance. Jennifer

Valtrex, which improved her symptoms after 4 days and resolved her symptoms after 8 days. *Id.* However, her symptoms recurred after eating certain foods, including Chinese, ranch dipping sauce, and anything with breaded batter. *Id.* After researching online, Petitioner tried avoiding glutamate in her diet. *Id.* She had a strong family history of epilepsy and wanted to be tested for seizure activity. *Id.* Petitioner stated to Dr. Mohiuddin that she was able to reduce the tics by moving her arms in a rhythmic motion. *Id.* On exam, Dr. Mohiuddin noted that Petitioner had no abnormal movements, tics, or phonetic grunting during the entire encounter. *Id.* At 5. Mohiuddin's assessment was that she had a tic disorder, "likely acquired with previous suspicion of an autoimmune component similar to PANS occurring later in life." *Id.* An EEG performed on July 29, 2013 was within normal limits. *Id.* At 7. A sleep study performed on September 9, 2013 was also normal. *Id.* At 11.

On August 12, 2013, Petitioner met with Dr. Lebel for a breast cancer predisposition consult. Pet'r's Ex. 10 at 12. Dr. Lebel wrote in his notes that he reviewed the positive findings on "NucSeek" testing, ordered by Dr. Trifiletti. *Id.* Dr. Lebel found that the NLN gene findings were "probably clinically significant." *Id.* At 13. He stated that these genes may be passed on to her children and place her children at risk of being similarly affected. *Id.* Dr. Lebel was unable to complete breast cancer predisposition testing due to cost and did no other independent testing of Petitioner. *Id.* At 22.

Petitioner returned to Dr. Mihaila on January 10, 2014. Pet'r's Ex. 10 at 25. Dr. Mihaila noted that Petitioner had no abnormal involuntary movements or vocalizations during the interview. *Id.* At 26. Petitioner reported Dr. Trifiletti's theory that the flu vaccine contained MSG, and given Petitioner's genetic predisposition to MSG intolerance, her "blood brain barrier was damaged." *Id.* At 25. There are no contemporaneous medical records from Dr. Trifiletti on the record documenting when he discussed this theory with Petitioner. According to Dr. Trifiletti, this blood brain barrier damage could cause the unusual movements to develop due to "excess of 'glutamine' released by actions of MSG." *Id.* Petitioner expressed an interest in having testing done on the integrity of the blood-brain barrier, suggesting an "MRI with glutamine added to the dye." *Id.* Dr. Mihaila explained that he did not have methods to test the integrity of the blood brain barrier, and maintained his original opinion that the tics had a non-organic cause. *Id.* At 26. Dr. Mihaila stated that he could not comment on the role of MSG in causing abnormal movements, nor the significance of any genetic findings and their link to MSG and abnormal movements. *Id.*

On July 17, 2015, Dr. Trifiletti authored a letter asserting that Petitioner has a movement disorder, which is "likely autoimmune/post[-]immune in nature." Pet'r's Ex. 6 at 13. He stated that Petitioner received an intra-nasal flu vaccine on September 25, 2012, and sixteen days later developed neurological symptoms. *Id.* Dr. Trifiletti also stated that Petitioner has been under his care since November 2012 and he had considered a diagnosis of PANDAS/PANS due to Petitioner's sudden onset of tics. *Id.* It is unclear from the medical records exactly how many

---

Frankovich, et al., *Multidisciplinary Clinic Dedicated to Treating Youth with Pediatric Acute-Onset Neuropsychiatric Syndrome: Presenting Characteristics of the First 47 Consecutive Patients*, 25 J CHILD ADOLESC. PSYCHOPHARMACOL. 38 (2015). PANS is thought to be caused by infection, inflammation or other trigger that is not specifically identified as streptococcus. *Id.*

visits Petitioner made to Dr. Trifiletti. Dr. Trifiletti stated in his letter that he "always considered it likely that the live flu mist vaccine . . . [was] related to [Petitioner]'s problems. *Id.* at 14. He also found "rare polymorphisms called PARP1 and POLG, [which] predispose to enhanced sensitivity to oxidative stress, such as that which would follow administration of a vaccination." *Id.* He concluded that Petitioner was genetically pre-disposed to a vaccination reaction, which led to her subsequent neurological symptoms. *Id.*

b. Expert Review

i. Petitioner's Expert, Dr. Rosario Trifiletti

Dr. Trifiletti is a pediatric neurologist at a private child neurology practice in Ramsey, New Jersey. ECF No. 35 at 4, filed Feb. 8, 2017. He received a medical degree from Johns Hopkins University School of Medicine in 1986, where he was a fellow in the Medical Scientist Training Program. *Id.* at 2. In 1986, he also received his Ph.D. in Pharmacology and Experimental Therapeutics at Johns Hopkins. Thereafter, he completed a two-year residency in the Department of Pediatrics at Columbia-Presbyterian Medical Center. *Id.* From 1988 to 1991, Dr. Trifiletti was a pediatric neurology fellow at the Neurological Institute of New York at the Columbia-Presbyterian Medical Center. *Id.*

Dr. Trifiletti served as the Chief of the Division of Child Neurology at the University of Medicine and Dentistry of New Jersey (UMDNJ) from 2003 to 2007, before working as a staff pediatrician and neurologist at Morristown Memorial and Overlook Hospitals from 2007 to 2009. *Id.* at 3. In addition, Dr. Trifiletti worked in academia in various professorships at The Neurological Institute of New York; Columbia-Presbyterian Medical Center; The New York Hospital-Cornell Medical Center; The New York Medical College; and UMDNJ. *Id.* He is board certified in pediatrics (with a re-certification pending) and neurology, with a special competence in child neurology. *Id.* at 2.

In a letter dated January 18, 2016, Dr. Trifiletti articulated his causation theory for Petitioner's movement disorder. Pet'r's Ex. 14 at 1-3. Dr. Trifiletti stated that a specific type of poly-ADP–ribose polymerase ("PARP") mutation can result in reduced function of the enzyme coded for by the PARP1 gene. *Id.* at 2. A PARP1 haploinsufficiency can occur and affect the enzyme's role in DNA repair. This malfunction, Dr. Trifiletti asserted, can lead to the development of tic disorders. *Id.* More specifically, Dr. Trifiletti asserted that a haploinsufficiency would reduce PARP1's ability to perform its role in regulating glutamate excitotoxicity. *Id.* Dr. Trifiletti noted that the flu vaccine contains 188 micrograms of glutamate. *Id.* Dr. Trifiletti concluded that the amount of glutamate in one dose of the live flu mist vaccine may not be properly regulated in an individual with this mutation and is "more than sufficient" to trigger glutamate excitotoxicity in someone with a haploinsufficiency. *Id.* at 2-3. Consequently, that person would be susceptible to biological effects resulting from glutamate excitotoxicity, including but not limited to tics. *Id.* Dr. Trifiletti mentioned to Dr. LaPointe that an NLN gene mutation can also relate to Tourette's, but Dr. Trifiletti does not discuss the implications of an NLN mutation in his causation theory.

Petitioner went to see Dr. Trifiletti after conducting research on her symptoms and possible diagnosis. Petitioner, a nurse, had developed a "sudden and otherwise medically-unexplained onset of tics," and Dr. Trifiletti initially believed her symptoms may have been consistent with a "possible diagnosis of PANDAS/PANS." *Id.* Dr. Trifiletti performed genetic sequencing on Petitioner and found two mutations that "predispose[d] [Petitioner] to enhanced sensitivity to oxidative stress." Additionally, Dr. Trifiletti noted that Petitioner's elevated IgG levels offer support that Petitioner may have suffered from a recurrent or chronic bacterial infection. *Id.*

Dr. Trifiletti ultimately opined that Petitioner developed TS because her genetic mutation lead to a PARP1 haploinsufficiency, which prevented the proper regulation of the glutamate present in the flu vaccine. *Id.* Dr. Trifiletti concluded that for Petitioner, this inability to regulate glutamate led to excitotoxicity, infection, and the onset of tics. Additionally, due to her (presumed) haploinsufficiency, Dr. Trifiletti had a reasonable suspicion that Petitioner suffered from an infection that was activated by the flu vaccine. *Id.* Dr. Trifiletti "always considered it likely" that Petitioner's receipt of the Flu vaccine, containing monosodium glutamate, "directly accounts for her symptoms." *Id.* at 2. As further evidence of his causation theory, Dr. Trifiletti notes "the replication of this phenomenon with ingestion of food containing MSG years later is explained by [Petitioner's] continued sensitivity to glutamate." *Id.* at 3.

ii. **Respondent's Expert, Dr. Donald Gilbert**

Dr. Donald Gilbert is currently a professor of pediatrics and neurology at Cincinnati Children's Hospital Medical Center, where he directs the Movement Disorders and Tourette Syndrome program. Resp't's Ex. B at 5, filed April 1, 2016. He received a medical degree from University of Michigan in Ann Arbor, Michigan in 1993. *Id.* at 2. He thereafter was an intern and resident in pediatrics at Johns Hopkins for two years before completing a residency in child neurology at Johns Hopkins in 1998. *Id.*

Dr. Gilbert has been on the faculty of Children's Hospital Medical Center University of Cincinnati since 1998, and worked as a physician at this institution's New Onset Epilepsy Program from 1998 to 2001. *Id.* at 3-4. He has also served as the Director of the Cincinnati Children's Hospital Medical Center Transcranial Magnetic Stimulation Laboratories since 2001 and heads the Cincinnati Children's Hospital Medical Center Child Neurology Residency Program. *Id.* at 2. Dr. Gilbert is board certified in neurology with special qualification in child neurology. *Id.* at 3.

Dr. Gilbert reviewed Dr. Trifiletti's causation theory and found it to be based on "inaccurate" biology and "wild speculation." Resp't's Ex. A. at 8. Dr. Gilbert disputed Dr. Trifiletti's assertion that one nucleotide mutation can significantly alter the PARP1 protein and change its function, ultimately causing disease in a patient. *Id.* at 8-9. Dr. Gilbert stated explicitly that "one mutation does not cause disease" and "there are two mutated genes that eliminate, or nearly eliminate, function of the protein to have disease." *Id.* At 8. Dr. Gilbert also noted Dr. Trifiletti's lack of research providing an empiric basis for his theory. *Id.* at 6-9. Dr. Trifiletti cited to a BRCA study, but Dr. Gilbert discounted this evidence as irrelevant, stating, "[i]t is well known that BRCA1 and BRCA2 mediate their effects via PARP1," but there is no

evidence that PARP1's role in the development of certain cancers is also seen in movement disorders. *Id.* at 9. Dr. Gilbert also took issue with Dr. Trifiletti's assessment of how the mutated gene would function. Dr. Gilbert opined that there is no evidence or information available that illustrates how this specific single amino acid change would affect the function of the protein, and specifically if it would lead to disease or movement disorders. *Id.* at 8-9.

Dr. Gilbert reviewed Petitioner's medical records and concluded that Petitioner suffered from "anxiety" and "developed a psychogenic movement disorder which was a physical symptom of anxiety." *Id.* at 11. Dr. Gilbert pointed out Petitioner's VAERS report, where she analogized her symptoms with the symptoms of "Desiree Jennings." *Id.* at 4. Dr. Gilbert then questioned whether Petitioner "knows that movement disorder neurologists who viewed the Desiree Jennings video thought that her dystonia was psychogenic, not auto-immune, not triggered by a flu vaccine." *Id.* Additionally, Dr. Gilbert questioned Dr. Lebel's remark that Petitioner's NLN gene mutation findings were "probably clinically significant." *Id.* at 6. Dr. Gilbert stated that it is unclear why Dr. Lebel thinks this, since there are "no reported neurological diseases related to mutations in this gene." *Id.*

Dr. Gilbert dismissed Dr. Trifiletti's theory that Petitioner suffered from any type of infection activated by the flu vaccine because Petitioner lacked "any symptoms that are likely to be post-infectious or auto-immune mediated." *Id.* at 5. Dr. Gilbert noted that "it is ideal to make judgments by seeing patients, not by reading about them;" however, Dr. Gilbert relied heavily on the notes of Petitioner's primary care physician, Dr. Williams, and the notes of movement disorder specialist Dr. Mihaila, "who saw the patient during her acute illness and made the diagnosis of conversion disorder." *Id.* at 9.

III. The Applicable Legal Standard

Vaccine Rule 8(d) provides that "[t]he special master may decide a case on the basis of written submissions without conducting an evidentiary hearing." Vaccine Rule 8(d). On July 8, 2016, Petitioner filed a Motion for Decision on the Record, sua sponte. Respondent filed a Response, arguing that Petitioner's case should be dismissed for insufficient proof.

To receive compensation under the Vaccine Act, Petitioner must demonstrate either that: (1) Petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at 42 U.S.C. § 300aa-14, as amended by 42 C.F.R. § 100.3; or (2) that she suffered an "off-Table Injury," one not listed on the Table as a result of her receipt of a covered vaccine. *See* 42 U.S.C. §§ 300aa-11(c)(1)(C); *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006). Petitioner does not allege a Table injury in this case; thus she must prove that her injury was caused-in-fact by a Table vaccine.

To establish causation-in-fact, Petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. 42 U.S.C. § 300aa-13(a)(1)(A). Petitioner is required to prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly v. Sec'y of Health & Human Servs.*,

592 F.3d 1315, 1321-22 (Fed. Cir. 2010) (*quoting Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)).

In the seminal case of *Althen v. Secretary of the Department of Health and Human Services*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278-79 (Fed. Cir. 2005). The *Althen* test requires the petitioner to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* To establish entitlement to compensation under the Program, Petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *See id.*

Specifically, under the first prong of *Althen*, Petitioner must offer a scientific or medical theory that answers in the affirmative the question "can the vaccine(s) at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004). This may be accomplished in a number of ways. "Reliability and plausibility of pathogenesis can be bolstered by providing evidence that at least a sufficient minority in the medical community has accepted the theory, so as to render it credible." *Id.* In addition, epidemiological studies and an expert's experience, while not dispositive, lend significant credence to the claim of reliability. *Id.* Articles published in respected medical journals, which have been subjected to peer review, are also persuasive. *Id.* However, publication "does not necessarily correlate with reliability," because "in some instances well-grounded but innovative theories will not have been published." *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 593–94 (1993).

In addition to showing that the vaccine at issue can cause a particular injury, a petitioner must also, under *Althen's* second prong, prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; the petitioner must explain "how and why the injury occurred." *Pafford*, 2004 WL 1717359, at *4.

While a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. For example, if the petitioner's theory involves a process that takes several days to develop after vaccination, an injury that occurred within a day of vaccination would not be temporally consistent with that theory. Conversely, if the theory is one that anticipates a rapid development of the reaction post-vaccination, the development of the alleged injury weeks or months post-vaccination would not be consistent with that theory. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Human Servs.*, 24 Cl. Ct. 400, 403-04 (Fed. Cl. Oct. 23, 1991); *see also Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992); *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983) (stating that inoculation is not the cause of every event that occurs within a ten-day period following it).

A petitioner who demonstrates by a preponderance of the evidence that he suffered an injury caused by vaccination is entitled to compensation, unless Respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994).

IV. Discussion[11]

a. *Althen* Prong One

Petitioners must offer a medical theory that answers in the affirmative "can the vaccine(s) at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Human Servs*., No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004). Based on a careful consideration of the evidence, I find nothing in Petitioner's record that provides a reliable medical theory of vaccine causation. Dr. Trifiletti reached unsupported conclusions and failed to present a coherent theory to explain how the flu vaccine, administered to an individual with unconfirmed PARP1 haploinsufficiency, causes a movement disorder to develop.

Dr. Trifiletti is a pediatric neurologist with no identified training in genetics, yet he has presented a novel causation theory based on genetic mutation. While it is not necessary that Dr. Trifiletti have a specialization in genetics to offer such a theory, the education and practice of an expert can add significant credibility to his opinion. Dr. Trifiletti stated in his opinion letter that his clinic has compiled a database with genetic sequencing from over 600 patients; however, he did not rely on any evidence within that database to assert that this mutation is a plausible impetus for a vaccine reaction that could result in the development of a tic disorder. Dr. Trifiletti noted that an unrelated patient underwent genetic testing and presented with the same PARP1 mutation as Petitioner, but Dr. Trifiletti does not state whether this individual also suffers from a glutamate sensitivity or developed a movement disorder.

In support of Dr. Trifiletti's theory, Petitioner provided several articles that discuss current research in genetic studies. But, these papers do not provide any link between the single mutation theory presented and the onset of TS. The Richer paper,[12] for example, discusses how treatment providers are attempting to understand how specific biological pathways can "contribute to the Tourette phenotype." Pet'r's App. Attach. to Ex. 14 at 12-17. However, Richer states that "the assumption that a single gene controls the tic phenotype was a pitfall on many genetic studies." *Id.* at 17. It also repeatedly refers to the heterogeneity of TS and the "genetic overlap between TS and other neuropsychiatric disorders." *See generally id.* The section that specifically details researcher interest in the connection between glutamatergic pathways and the development of TS focuses on the comorbidity of TS and obsessive-

[11] The undersigned has reviewed all of the medical literature provided by the parties, but will only discuss the literature relevant to this decision.

[12] Richer P, Fernandez TV, *Tourette Syndrome: Bridging the Gap between Genetics and Biology*, 1 MOLECULAR NEUROPSYCHIATRY 156-64 (2015).

compulsive disorder, and their shared genetic and pathophysiological backgrounds. *See id.* at 20. Dr. Trifiletti's theory simply does not include a neuropsychiatric component.

The remaining literature[13] Petitioner filed contains information related to genetic mutations for unrelated diseases or seems to run counter to Petitioner's claim by suggesting that a haploinsufficiency would lead to reduced excitotoxicity. *Id.* at 1-11. While petitioners and their experts are not expected to present theories backed with scientific certainty, *see Althen*, 418 F.3d at 1279-80, the expert must provide some details that allow the theory to be evaluated. *See W.C. v. Sec'y of Health and Human Servs.*, 704 F.3d 1352, 1360-61 (Fed. Cir. 2013) (holding special master was not arbitrary and capricious in rejecting petitioner's theory); *Hines v. Sec'y of Health and Human Servs.*, 21 Cl. Ct. 634, 646 (1990) (ruling that a special master may give little weight to a doctor's conclusory affidavit), *aff'd on irrelevant grounds*, 940 F.2d 1518 (Fed. Cir. 1991). Dr. Trifiletti's theory lacks a cogent argument explaining how a potential PARP1 mutation would lead to glutamate excitotoxicity and TS following the administration of a flu vaccine.

b. *Althen* Prong Two

The second prong of *Althen*, the requirement for a logical sequence of cause and effect between the vaccine and the injury, has been characterized as addressing the "did it cause?" or specific causation query. *See Pafford*, 2004 WL 1717359 at *4. In other words, even if a vaccine can cause the injury alleged, Petitioner must show that it did so in her case. Because I do not find that Dr. Trifiletti successfully articulated how the FluMist vaccine can cause TS, Petitioner's application of Dr. Trifiletti's theory to her injuries is also unpersuasive.

Petitioner was seen by her primary care physician, Dr. Williams, and emergency room doctor, Dr. Izadyar, immediately after the onset of her symptoms in October of 2012. Dr. Williams prescribed Petitioner anti-anxiety medication for treatment of her tic, and Dr. Izadyar was unable to rule out a somatoform disorder. Petitioner was also seen by Dr. LaPointe, who noted that a psychiatrist at Upstate Hospital saw Petitioner and diagnosed her with conversion disorder. Petitioner saw several other physicians in the subsequent years in attempt to better understand her injury and its cause; yet of the numerous physicians who diagnosed Petitioner, only Dr. Trifiletti definitely ruled out psychiatric causation. Dr. Williams referred Petitioner to movement specialist, Dr. Mihaila, who initially characterized Petitioner's condition as a "tic like movement disorder that is mostly likely a conversion disorder." Pet'r's Ex. 10 at 8. Petitioner eventually returned to Dr. Mihaila after seeing Dr. Trifiletti. Even after review of Dr. Trifiletti's report and Petitioner's additional medical records and tests, Dr. Mihaila stated, "I cannot

[13] Wang X, Liu L, et al., *Haploinsufficiency of Parp1 accelerates Brca1-associated centrosome amplification, telomere shortening, genetic instability, apoptosis, and embryonic lethality*, 14 CELL DEATH AND DIFFERENTIATION 924-31 (2007); Yang W, Sevigny M, et al., *Poly(ADP-ribose) glycohydrolase mediates oxidative and excitotoxic neuronal death*, 98 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES 12227-32 (2001).

comment on the speculations of the role of MSG in causing abnormal movements. I maintained my opinion that what I saw one year ago were non-organic movement disorders." Pet'r's Ex. 10 at 26.

I find Dr. Mihaila's records and Dr. Gilbert's assessment persuasive. Dr. Trifiletti's characterization of a causal relationship between Petitioner's flu vaccination and Tourette's is conclusory, and does not include an explanation for how the vaccine actually caused Petitioner's movement disorder. The majority of medical evidence in this case supports that Petitioner suffers from a psychogenic disorder due to psychological stressors and not a reaction to the flu vaccination.

c. *Althen* Prong Three

The lack of detail on the theory carries over to create a deficiency with respect to the third *Althen* prong, which concerns timing. This element requires a persuasive showing of a defined period of time during which an inference of causation may be drawn appropriately. *Shapiro v. Sec'y of Health and Human Servs.*, 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.* 503 Fed. Appx. 952 (Fed. Cir. 2013). However, a mere showing of a proximate temporal connection between a vaccination and an injury is insufficient, standing alone, to establish causation. *Grant v. Sec'y of Health and Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). Although arguably, Dr. Trifiletti's diagnosis does speak to a temporal relationship between Petitioner's vaccination and subsequent injury, the two events occurring in quick succession is not sufficient to establish entitlement to compensation. Dr. Trifiletti does not include any description of appropriate onset for vaccine-induced T.S. He does not explain how the period of time between Petitioner's vaccination and the onset of her symptoms would be evidence of a causal relationship. Except to state that the time period between vaccine and onset was sixteen days, he does not discuss timing at all in his "attempt to outline the biological and medical plausibility of [his] thesis that monosodium glutamate in the Flu-Mist vaccine directly accounts for [Petitioner's] symptoms." Pet'r's Ex. 14 at 2. Petitioner has not provided sufficient evidence to establish that the timing of her injury fits within a plausible causal theory.

d. Alternative Cause

Respondent has not proposed an alternative cause and asserted that Petitioner did not meet "her statutory burden of establishing a prima facie case for entitlement, [so] the burden never shift[ed] to Respondent to prove an alternative cause." Response at 6. *See LaLonde v. Sec'y of Health and Human Servs*., 746 F.3d 1334, 1340-40 (Fed. Cir. 2014). The undersigned agrees. Petitioner has not provided preponderant evidence to establish that but for the vaccination, Petitioner's TS would not have developed and that the vaccination was a significant factor in bringing about her condition.

V. Conclusion

For the reasons discussed above, Petitioner has not established entitlement to compensation. Accordingly, Petitioner's Motion for a Decision on the Record is GRANTED, and the petition is DISMISSED for insufficient proof. The Clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

/s/ Herbrina D. Sanders
Herbrina D. Sanders
Special Master